



UNITED STATES PATENT AND TRADEMARK OFFICE

c/k

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,180	03/20/2006	Blas Cerda	NEN-23002/16	2257
37742	7590	08/02/2007		
GIFFORD, KRASS, SPRINKLE, ANDERSON & CITKOWSKI, P.C. P.O. BOX 7021 TROY, MI 48007-7021			EXAMINER MARTIN, PAUL C	
			ART UNIT 1657	PAPER NUMBER
			MAIL DATE 08/02/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/539,180	Applicant(s) CERDA, BLAS	
	Examiner Paul C. Martin	Art Unit 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 June 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/26/06, 10/26/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-40 are pending in this application.

Election/Restrictions

Applicant's election without traverse of the Species (metabolically indicative enzyme: hydrolase) in the reply filed on 07/17/07 is acknowledged. The elected species is acknowledged to read on all of the claims.

Claims 1-40 were examined on their merits.

Drawings

The drawings are objected to as failing to comply with 37.CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: A-F. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended.

Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The use of the trademark Complete™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Double Patenting

Statutory

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter.

See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970). A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-27, 30-33 and 37-40 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-28, 45-47 and 54-57 of copending Application No. 10/539273. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Non-Statutory

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s).

See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 10, 19-21, 23, 24, 27 and 37 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 7, 12, 14-18 and 20-26 of copending Application No. 10/652,732.

Although the conflicting claims are not identical, they are not patentably distinct from each other. The method for detecting a suspected inborn error of metabolism in a neonate/newborn/child of '180; comprising contacting a dried blood sample, the sample comprising one or more metabolically indicative enzymes and one or more metabolic analytes, with one or more substrates in the presence of one or more protease inhibitors, contacting the mixture with a reagent that inhibits the enzyme and determining the presence or amount of one or more metabolic analytes and at least one enzymatic reaction product using tandem mass spectrometry, wherein the determined presence or amount of one or more metabolic analytes and at least one enzymatic product correlates with the presence or absence of a metabolic disorder (Claims 1-8, 10 and 27). Further, '180 teaches contacting the sample at various times in the method with one or more reference substrates, products or analytes (Claims 18-21) and wherein the non-aqueous reaction mixture comprises an organic solvent (Claims 23 and 24).

The method of '180 would have been recognized by one of ordinary skill in the art as obvious over the method of '732, which describes a method for screening of inborn errors of metabolism in a newborn by tandem mass spectrometry comprising contacting a dried blood sample with a polar solvent, the sample comprising at least one polar and non-polar analyte and at least one enzyme, with exogenous substrate for the at least one enzyme, adding internal standard for the enzymatic product, polar and non-polar analyte(s) and determining the amounts of the polar, non-polar analyte(s) and enzymatic product wherein the measured amounts are indicative of the presence or absence of an inborn error of metabolism in the newborn (Claims 1-5, 7, 12, 14-18 and 22). One of ordinary skill in the art would have recognized that although the two methods vary slightly in construction and methodology, the variations are superficial in nature (i.e., that organic solvents can be either polar or non-polar and that reference standards are added at different time periods in the methods) and do not materially change the outcomes of the two methods.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 36-40 have been renumbered 35-39.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzyme mediated metabolic disorders with corresponding metabolic analytes listed in the Specification, Pgs. 20-21, does not reasonably provide enablement for the detection of any metabolic disorder in an individual, or any metabolic disorder that does not have both metabolically indicative enzymes and analytes.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 58 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention.

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Nature of the Invention:

The instant invention is directed toward the detection of a metabolic disorder in an individual comprising the detection of the presence or amount of one or more metabolic analytes and the presence or amount of at least one enzyme product.

Presence or Absence of Working Examples:

The sole working example is directed to the simultaneous determination of the amount of biotinidase (enzyme)/biocytin(substrate) reaction product (presumably biotin and/or lysine) and the endogenous metabolic analytes acylcarnitines and α -amino acids.

Amount of Direction or Guidance presented:

The disclosure broadly defines a "metabolic disorder" as any condition that interferes with normal creation or destruction of biological molecules that regulate health. However the claims and teachings of the instant disclosure are directed only to those metabolic disorders having both detectable metabolic analytes and enzymatic reaction products. The Applicants disclosure does not teach or suggest how one of ordinary skill in the art will detect a metabolic disorder in an individual if the metabolic disorder is not characterized by metabolically indicative enzymes and metabolic analytes.

Breadth of the Claims:

The claims are broadly drawn to the detection of any metabolic disorder in an individual comprising the detection of the presence or amount of one or more unspecified metabolic analytes and the presence or amount of at least one unspecified enzyme product.

The State of the Prior Art:

As stated above, the instant invention is drawn to the detection of any metabolic disorder relying upon the detection of the presence or amount of one or more unspecified metabolic analytes and the presence or amount of at least one unspecified enzyme product. However, it is known in the Art that certain metabolic disorders are not characterized by both metabolic analytes and enzyme-mediated reaction products.

For example, Gahl *et al.* teaches the metabolic disorder cystinosis, a lysosomal storage disease that results from the impaired transport of cystine, usually through a mutation in the gene for cystinosis (Pg. 114, Column 2, Lines 3-4 and Pg. 115, Column 1, Lines 25). The Merck Manual Home Index teaches that the metabolic disorder Alkalosis, excessive blood alkalinity is caused by either a loss of acid from the blood or an overabundance of bicarbonate in the blood. Neither of these two metabolic disorders are characterized by both metabolically indicative enzymes and analytes and thus could not be detected in an individual using the instant invention.

For all of the reasons above, the instant disclosure does not reasonably provide enablement for the detection of any metabolic disorder in an individual, or any metabolic disorder that does not have both metabolically indicative enzymes and analytes. Therefore the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28 and 34, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 28 and 34 contain the trademark/trade name Complete™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982).

The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a protease inhibitor composition and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-13, 17-29, 37, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerber *et al.* (2001) in view of Roe *et al.* (1999) and Guerra-Giraldez *et al.* (2002).

Gerber *et al.* teaches a method for detecting the inborn lysosomal Storage disease, Sanfilippo syndrome in individuals, by contacting a fibroblast sample containing Sanfilippo enzymes A-D with substrates for enzymes A-D (α -2-deoxy-2-N-sulfonamidoglucosamine sulfamidase, α -2-deoxy-2-N-acetylglucosamine hydrolase, acetyl-coenzyme A: α -2-deoxy-2-aminoglucosamine transferase and α -2-deoxy-2-N-acetylglucosamine-6-sulfate sulfatase) to produce a reaction mixture, under conditions wherein the enzymes are capable of acting on their corresponding substrate to generate a product; contacting the reaction mixture with ice water which inhibits the ability of the enzymes to act on their corresponding substrates, adding internal product standards to the appropriate reaction mixtures; wherein the reaction products are soluble in the ice water; to produce a test sample and determining the presence and relative amounts of the enzyme reaction products using mass spectrometry wherein the determined presence or relative amounts of the products contained in the test sample correlates with the presence of Sanfilippo syndrome (Pg. 1653, Column 2, Lines 28-54 and Pg. 1654, Column 1, Lines 9 and Pg. 1655, Fig. 2).

Gerber *et al.* teaches that the use of mass spectrometry for biomedical applications is now possible with the development of electrospray and matrix-assisted laser desorption/ionization methods, which have proven applicable to virtually all biological metabolites examined to date (Citation #10, Roe *et al.*) (Pg. 1652, Column 1, Lines 8-12).

Gerber *et al.* does not teach the detection of a metabolic disorder in an individual by simultaneous detection of the presence or amount of one or more metabolic analytes contained in a sample, wherein the sample is in a vessel, separating a sample into two portions and performing the method on each portion, wherein the individual is a neonate/newborn, child or adult, wherein the metabolic analyte is an acylcarnitine or plurality of acylcarnitines, contacting the sample with one or more reference substrates, prior to determining, adding one or more reference analytes corresponding to one or more metabolic analytes, wherein the reagent is methanol, wherein the metabolic disorder is acquired, or the use of the protease inhibitors Pepstatin or Complete™ protease cocktail.

Roe *et al.* teaches the detection of suspected inherited metabolic disorders in individuals (Pg. 245, Column 1, Lines 42-45 and Column 2, Lines 8) wherein cultured fibroblasts are mixed with analyte internal standard in a vessel, extracted with absolute ethanol, and reconstituted in methanol/glycerol prior to analysis by electrospray or tandem mass spectrometry wherein a plurality of acylcarnitines are determined (Pg. 244, Column 2, Lines 32-52), and wherein the individuals are neonates/infants or adults (PG. 245, Column 2, Lines 35-44).

Guerra-Giraldez *et al.* teaches the use of Complete™ protease inhibitor cocktail in enzyme assays involving cell lysate (Pg. 2652, Column 2, Lines 16-19).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the enzymatic product metabolic disorder detection method of Gerber *et al.* with the metabolic analyte detection method of Roe *et al.* because both methods are directed to the detection of metabolic disorders in individuals.

It would have been obvious to one of ordinary skill in the art at the time of the invention to separate the sample into two portions (duplication of parts) because the MPEP states: *In re Harza*, 274 F.2d 669, 124 USPQ 378 (CCPA 1960) (Claims at issue were directed to a water-tight masonry structure wherein a water seal of flexible material fills the joints which form between adjacent pours of concrete.

The claimed water seal has a "web" which lies ** in the joint, and a plurality of "ribs" ** >projecting outwardly from each side of the web into one of the adjacent concrete slabs. <The prior art disclosed a flexible water stop for preventing passage of water between masses of concrete in the shape of a plus sign (+). Although the reference did not disclose a plurality of ribs, the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced.). It would have been obvious to one of ordinary skill in the art to modify the methods of Gerber *et al.* and Roe *et al.* to the use of protease inhibitors such as Complete™ protease inhibitor cocktail or pepstatin because the use of protease inhibitors was well-known at the time of the instant invention as a means of preventing protein degradation in cell lysate prior to analysis.

Combinations of protease inhibitors and individual protease inhibitors are routinely used in the art wherein cell lysate and proteins are assayed.

It would have been obvious to one of ordinary skill in the art to contact the sample with one or more reference substrates because the substrates would act as a verification control that the enzymes present were functioning in the same manner to generate the sample and reference products. One of ordinary skill in the art would have been motivated to combine these two methods because those of skill in the art would have recognized the suitability of combining two art recognized methods for detecting metabolic disorders in one assay.

Further, Roe *et al.* is specifically cited by Gerber *et al.* as teaching the use of mass spectrometry in the analysis of all biological analytes examined to date. It would have been obvious to one of ordinary skill in the art to apply the metabolic disorder detection methods of Gerber *et al.* and Roe *et al.* to the detection of acquired metabolic disorders because the method of Gerber *et al.* is clearly applicable to screening adults and would therefore encompass late-onset (acquired) forms of metabolic disorders. There would have been a reasonable expectation of success in making this combination because both methods are directed to the detection of metabolic disorders and because Gerber *et al.* suggests the use of mass spectrometry to analyze metabolic analytes.

Claims 1-13 and 16-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerber *et al.* (2001) in view of Roe *et al.* (1999) and Guerra-Giraldez *et al.* (2002) and further in view of Chace *et al.* (2001).

The teachings of Gerber *et al.*, Roe *et al.* and Guerra-Giraldez *et al.* were discussed above.

Neither Gerber *et al.* nor Roe *et al.* or Guerra-Giraldez *et al.* taught wherein the sample is a dried blood sample, wherein the metabolic analyte is one or more amino acids, or wherein the enzyme substrates are contained in dried form in the reaction vessels.

Chace *et al.* teaches a method of detecting a metabolic disorder in an individual wherein dried blood samples from newborns and infants are placed in vessels, standard solutions of acylcarnitines and amino acids are added to the samples in methanol prior to determination, and analyzed using tandem mass spectrometry (MS) to detect the presence and amount of acylcarnitines and a plurality of amino acids (Pg. 1168, Column 1, Lines 1-33 and Pg. 1171, Fig. 2 and Pg. 1173, Fig. 4).

Chace *et al.* teaches that the use of electrospray MS is advantageous over other biochemical tests which used MS/MS to quantify acylcarnitines and acylglycines in blood, urine and bile and which require complex interpretation and specialized protocols (Pg. 1167, Column 1, Lines 34-45) and that the dried blood spot technique is inexpensive when coupled to high volume automated analysis for newborn or high-risk screening (Pg. 1167, Column 2, Lines 15-22).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the enzymatic product metabolic disorder detection method of Gerber *et al.* and the metabolic analyte detection method of Roe *et al.* with the use dried blood samples from newborns and infants and analysis of amino acid levels because all the methods are directed to the detection of metabolic abnormalities in enzyme mediated disorders by mass spectrometry. One of ordinary skill in the art would have recognized that the placement of dried enzyme substrates in the reaction vessels would have been an obvious means of increasing efficiency of the method. The use of prepackaged and prepared assays containing dry reagents or ingredients would have been well within the purview of one of ordinary skill in the art. One of ordinary skill in the art would have been motivated to make these modifications because of the advantages of using dried bodily fluid samples, such as stability of the sample and substrates in dry form, ease of transport, as well as the in-expense and ease of coupling to automated high-throughput analysis as taught by Chace *et al.* above.

There would have been a reasonable expectation of success in making these modifications because all three methods are directed to the detection of inborn enzyme mediated metabolic disorders in individuals through mass spectroscopy analysis.

Allowable Subject Matter

Claims 14 and 15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

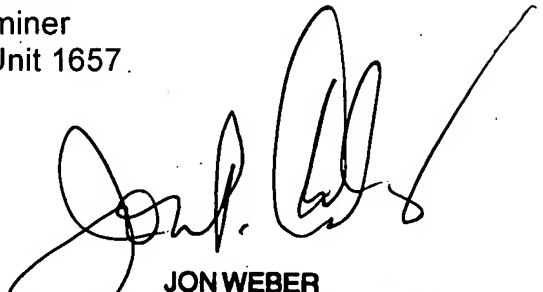
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1657

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

7/25/07



JON WEBER
SUPERVISORY PATENT EXAMINER